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SESSION RESUMED IN FILE 'REGISTRY' AT 07:52:11 ON 24 NOV 2004
FILE 'REGISTRY' ENTERED AT 07:52:11 ON 24 NOV 2004
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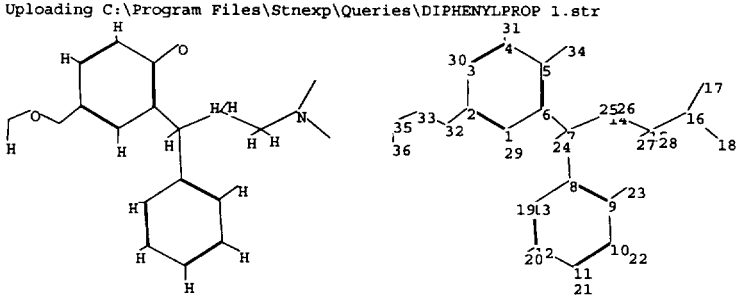
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.84	1.05

=>
Uploading C:\Program Files\Stnexp\Queries\DIPHENYLPROP 1.str

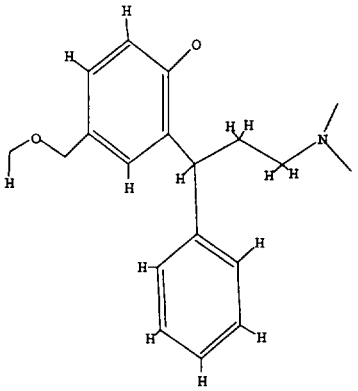


chain nodes :
7 14 15 16 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 36
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 13
ring/chain nodes :
17 18 35
chain bonds :
1-29 2-32 3-30 4-31 5-34 6-7 7-8 7-14 7-24 9-23 10-22 11-21 12-20
13-19 14-15 14-25 14-26 15-16 15-27 15-28 16-17 16-18 32-33 33-35 35-36
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13
exact/norm bonds :
5-34 15-16 16-17 16-18 32-33 33-35
exact bonds :
1-29 2-32 3-30 4-31 6-7 7-8 7-14 7-24 9-23 10-22 11-21 12-20 13-19
14-15 14-25 14-26 15-27 15-28 35-36
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS

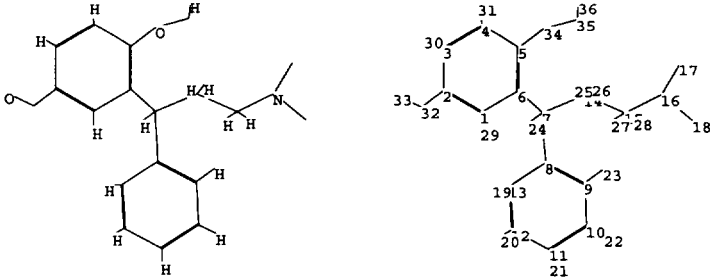
L3 STRUCTURE UPLOADED

=> D L3
L3 HAS NO ANSWERS
L3 STR



Structure attributes must be viewed using STN Express query preparation.

=>
Uploading C:\Program Files\Stnexp\Queries\DIPHENYLPROP 2.str



chain nodes :
7 14 15 16 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 36
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 13
ring/chain nodes :
17 18 35
chain bonds :
1-29 2-32 3-30 4-31 5-34 6-7 7-8 7-14 7-24 9-23 10-22 11-21 12-20
13-19 14-15 14-25 14-26 15-16 15-27 15-28 16-17 16-18 32-33 34-35 35-36

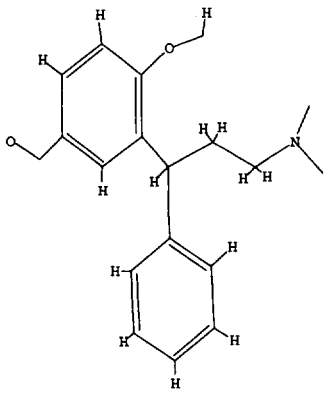
STN SEARCH TRANSCRIPT 10/17/05

ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13
exact/norm bonds :
5-34 15-16 16-17 16-18 32-33 34-35
exact bonds :
1-29 2-32 3-30 4-31 6-7 7-8 7-14 7-24 9-23 10-22 11-21 12-20 13-19
14-15 14-25 14-26 15-27 15-28 35-36
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS

L4 STRUCTURE UPLOADED

=> D L4
L4 HAS NO ANSWERS
L4 STR



Structure attributes must be viewed using STN Express query preparation.

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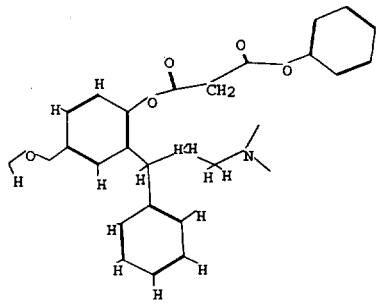

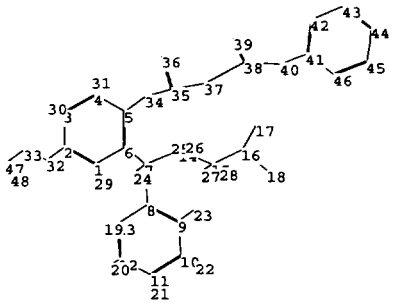

chain nodes :
7 14 15 16 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 36
37 38 39 40 47 48
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 13 41 42 43 44 45 46
ring/chain nodes :
17 18 35
chain bonds :
1-29 2-32 3-30 4-31 5-34 6-7 7-8 7-14 7-24 9-23 10-22 11-21 12-20
13-19 14-15 14-25 14-26 15-16 15-27 15-28 16-17 16-18 32-33 33-47 34-35
35-36 35-37 37-38 38-39 38-40 40-41 47-48
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13 41-42 41-46
42-43 43-44 44-45 45-46
exact/norm bonds :
5-34 15-16 16-17 16-18 32-33 33-47 34-35 35-36 38-39 38-40 40-41
exact bonds :
1-29 2-32 3-30 4-31 6-7 7-8 7-14 7-24 9-23 10-22 11-21 12-20 13-19
14-15 14-25 14-26 15-27 15-28 35-37 37-38 47-48
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13 41-42 41-46
42-43 43-44 44-45 45-46

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:Atom 42:Atom
43:Atom 44:Atom 45:Atom 46:Atom 47:CLASS 48:CLASS

L5 STRUCTURE UPLOADED

=> D L5
L5 HAS NO ANSWERS
L5 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> S L3 SSS FULL
FULL SEARCH INITIATED 07:54:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 197 TO ITERATE

100.0% PROCESSED 197 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

L6 25 SEA SSS FUL L3

=> S L4 SSS FULL
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FULL SCREEN SEARCH COMPLETED - 83 TO ITERATE

100.0% PROCESSED 83 ITERATIONS 24 ANSWERS
SEARCH TIME: 00.00.01

L7 24 SEA SSS FUL L4

=> S L5 SSS FULL
FULL SEARCH INITIATED 07:54:22 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 23 TO ITERATE

100.0% PROCESSED 23 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L8 0 SEA SSS FUL L5

=> S L6 OR L7 OR L8
L9 44 L6 OR L7 OR L8

=> FILE CAPLUS
COST IN U.S. DOLLARS SINCE FILE ENTRY 467.52 TOTAL SESSION 467.73

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 07:54:39 ON 24 NOV 2004
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FILE COVERS 1907 - 24 Nov 2004 VOL 141 ISS 22
FILE LAST UPDATED: 23 Nov 2004 (20041123/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

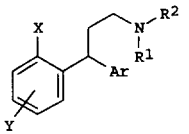
=> S L9
L10 8 L9

=> D 1-8 IBIB ABS HITSTR

L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:51413 CAPLUS
DOCUMENT NUMBER: 136:102178
TITLE: Preparation of 3,3-diarylpropylamines via hydroformylation-amination of diarylethenes in presence of a transition metal catalyst
INVENTOR(S): Donsbach, Martin; Eilbracht, Peter; Buss, Christian; Schmidt, Andreas
PATENT ASSIGNEE(S): Schwarz Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004399	A1	20020117	WO 2001-EP7803	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10033016	A1	20020124	DE 2000-10033016	20000707
EP 1299342	A1	20030409	EP 2001-962840	20010706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502748	T2	20040129	JP 2002-509068	20010706
US 2004034080	A1	20040219	US 2003-332290	20030714
US 6809225	B2	20041026		

PRIORITY APPLN. INFO.: DE 2000-10033016 A 20000707
WO 2001-EP7803 W 20010706
OTHER SOURCE(S): CASREACT 136:102178; MARPAT 136:102178
GI



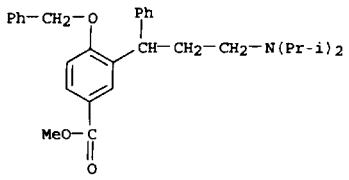
I

AB The invention relates to a novel method for producing 3,3-diarylpropylamines I [Ar = (un)substituted aryl; X = (un)substituted OH; Y = Cl, Br, I, CN, CH2OR, CHO, CO2H, CO2R; R = alkyl, aryl; R1, R2 = alkyl, cycloalkyl; NR1R2 = heterocyclic] by hydroformylation/hydrocarbonylation and subsequent reductive amination using a transition metal catalyst. Thus, 5,2-Me(HO)C6H3COPh was methylated and methylenated with MeP+Ph3 Br- to give 5,2-Me(MeO)C6H3CPh:CH2 which was treated with (Me2CH)2NH, CO, and H in presence of Rh(acac)(CO)2 and Bu3P to give 85% 5,2-Me(MeO)C6H3CHPhCH2CH2N(CHMe2)2.

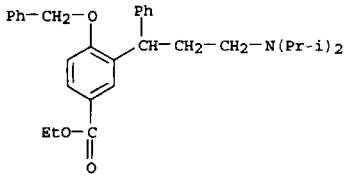
IT **286930-05-0P 389068-25-1P**

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 3,3-diarylpropylamines via hydroformylation-amination of diarylethenes in presence of a transition metal catalyst)

RN 286930-05-0 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)



RN 389068-25-1 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:923742 CAPLUS
DOCUMENT NUMBER: 136:37403
TITLE: Shortened synthesis of 3,3-diarylpropylamine derivatives
INVENTOR(S): Meese, Claus
PATENT ASSIGNEE(S): Schwarz Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096279	A1	20011220	WO 2001-EP6577	20010611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10028443	C1	20020529	DE 2000-10028443	20000614
CA 2412047	AA	20011220	CA 2001-2412047	20010611
EP 1289929	A1	20030312	EP 2001-947355	20010611
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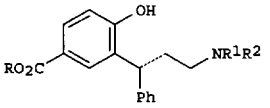
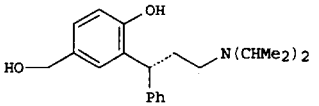
BR 2001011266	A	20031216	BR 2001-11266	20010611
JP 2004503520	T2	20040205	JP 2002-510423	20010611
NZ 521265	A	20040625	NZ 2001-521265	20010611
ZA 2002007204	A	20030523	ZA 2002-7204	20020909
US 2003212292	A1	20031113	US 2002-297778	20021209
US 6809214	B2	20041026		
NO 2002005967	A	20021212	NO 2002-5967	20021212

PRIORITY APPLN. INFO.: DE 2000-10028443 A 20000614
WO 2001-EP6577 W 20010611

OTHER SOURCE(S): CASREACT 136:37403; MARPAT 136:37403
GI



I

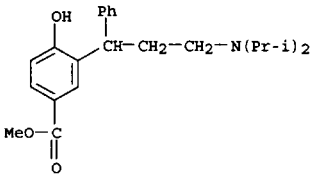


II

AB 3,3-Diarylpropylamines I [R = H, alkyl; R1, R2 = alkyl] are prepared by reaction of RO2CC6H4OH-4 with PhCH:CHCO2H to give a 2-oxo-4-phenyl-3,4-dihydrobenzopyran-6-carboxylate which is resolved via its cinchonidine salt, the (R)-isomer hydrolyzed to the acid which is reesterified, reduced to the benzopyranol, and subjected to aminolysis to give I. I [R = Me, R1, R2 = CHMe2], thus obtained, was then reduced to the benzyl alc. II.

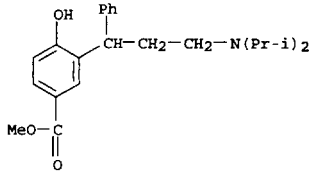
IT **214601-16-8P 380636-45-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(shortened synthesis of 3,3-diarylpropylamine derivs.)

RN 214601-16-8 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



RN 380636-45-3 CAPLUS

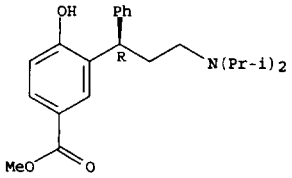
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **214601-17-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(shortened synthesis of 3,3-diarylpropylamine derivs.)
RN 214601-17-9 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:449738 CAPLUS
DOCUMENT NUMBER: 135:61141
TITLE: Preparation of stable salts of 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl esters.
INVENTOR(S): Meese, Claus
PATENT ASSIGNEE(S): Schwarz Pharma A.-G., Germany
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

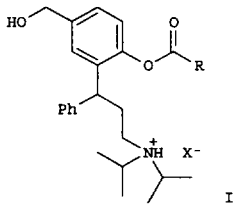
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19955190	A1	20010621	DE 1999-19955190	19991116
DE 29923134	U1	20000803	DE 1999-29923134	19991116
CA 2389749	AA	20010525	CA 2000-2389749	20001115
WO 2001035957	A1	20010525	WO 2000-EP11309	20001115
WO 2001035957	A3	20011227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001026667	A5	20010530	AU 2001-26667	20001115
BR 2000015610	A	20020730	BR 2000-15610	20001115
EP 1230209	A2	20020814	EP 2000-989857	20001115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003514018	T2	20030415	JP 2001-537950	20001115
ZA 2002003315	A	20030725	ZA 2002-3315	20020425
NO 2002002314	A	20020515	NO 2002-2314	20020515

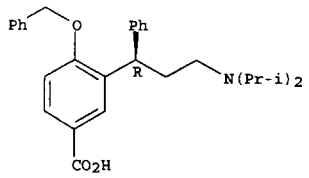
PRIORITY APPLN. INFO.: DE 1999-19955190 IA 19991116
WO 2000-EP11309 W 20001115

OTHER SOURCE(S): MARPAT 135:61141
GI



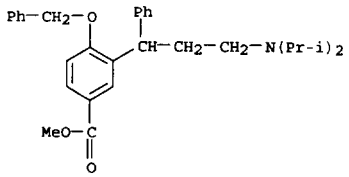
AB Title compds. [I; R = alkyl, cycloalkyl, (substituted) Ph; X- = residue of a physiol. acceptable (in)organic acid], were prepared Thus, (R)-2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl isobutyrate (II) (preparation given) in 2-butanone was treated with fumaric acid under warming to give 83.1% II.hydrogen fumarate.
IT **156755-33-8 286930-05-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of stable salts of 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl esters)
RN 156755-33-8 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

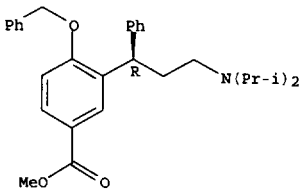
RN 286930-05-0 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)



IT **156755-35-0P 156755-37-2P 214601-16-8P 214601-17-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of stable salts of 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl esters)

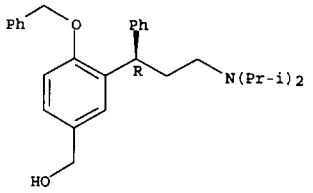
RN 156755-35-0 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

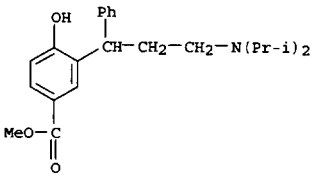


RN 156755-37-2 CAPLUS
CN Benzenemethanol, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

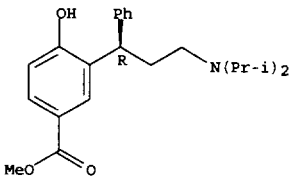


RN 214601-16-8 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



RN 214601-17-9 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

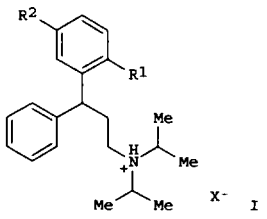
Absolute stereochemistry. Rotation (-).



L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:533448 CAPLUS
DOCUMENT NUMBER: 133:155419
TITLE: Stable salts of novel derivatives of 3,3-diphenylpropylamines
PATENT ASSIGNEE(S): Schwarz Pharma A.-G., Germany
SOURCE: Ger. Gebrauchsmusterschrift, 37 pp.
CODEN: GGXXFR
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 29923134	U1	20000803	DE 1999-29923134	19991116

DE 19955190 A1 20010621 DE 1999-19955190 19991116
PRIORITY APPLN. INFO.: DE 1999-19955190 IA 19991116
OTHER SOURCE(S): MARPAT 133:155419
GI

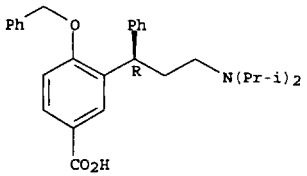


AB 3,3-Diphenylpropylamine salts I [R1 = RCO2; R = C1-6 alkyl, C3-10 cycloalkyl, (substituted) Ph; R2 = CH2OH; X = inorg. or organic acid] are prepared for use as prodrugs of agents for treatment of urinary incontinence and other spasmogenic disorders. I show improved absorption through biol. membranes and improved metabolic patterns and are easily crystallized I are prepared from I free base (R1 = PhCH2O, R2 = CO2Me) by debenzylation, reduction, acylation, and combination with HX. Thus, R-(-)-I-HCl (R1 = PhCH2O, R2 = CO2H) was esterified by refluxing in acidic MeOH, the ester was reduced with LiAlH4, the resulting carbinol was reduced with Raney Ni/H2, and the product [R-(+)-I free base, R = CHMe2] was converted to its H fumarate salt by heating with equimolar fumaric acid in 2-butanone; the salt was crystallized by addition of cyclohexanone and cooling to 0°.

IT **156755-33-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(stable salts of novel derivs. of diphenylpropylamines)

RN 156755-33-8 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

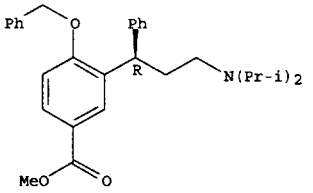


● HCl

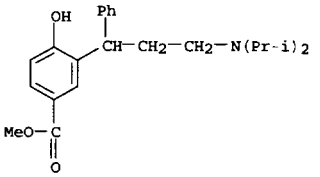
IT **156755-35-0P 214601-16-8P 214601-17-9P 286930-05-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stable salts of novel derivs. of diphenylpropylamines)

RN 156755-35-0 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

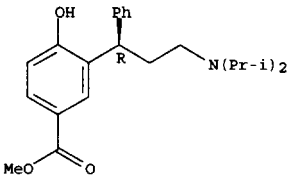


RN 214601-16-8 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

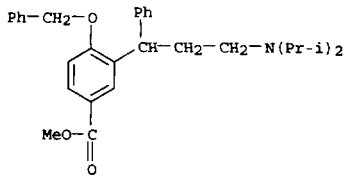


RN 214601-17-9 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 286930-05-0 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:736261 CAPLUS
DOCUMENT NUMBER: 131:336818
TITLE: Preparation of 3,3-diphenylpropylamines as antimuscarinic agents.
INVENTOR(S): Sparf, Bengt; Meese, Claus O.
PATENT ASSIGNEE(S): Schwarz Pharma AG, Germany
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 957073	A1	19991117	EP 1998-108608	19980512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2328920	AA	19991118	CA 1999-2328920	19990511
WO 9958478	A1	19991118	WO 1999-EP3212	19990511
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941412	A1	19991129	AU 1999-41412	19990511
AU 748057	B2	20020530		
BR 9910406	A	20010109	BR 1999-10406	19990511
EP 1077912	A1	20010228	EP 1999-924929	19990511
EP 1077912	B1	20020703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200003319	T2	20011221	TR 2000-200003319	19990511
AT 220056	E	20020715	AT 1999-924929	19990511
EP 1254890	A1	20021106	EP 2002-13481	19990511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NZ 507487	A	20021126	NZ 1999-507487	19990511
PT 1077912	T	20021129	PT 1999-924929	19990511
ES 2181443	T3	20030216	ES 1999-924929	19990511
RU 2199525	C2	20030227	RU 2000-125813	19990511
JP 2003519079	T2	20030617	JP 2000-548284	19990511
ZA 2000005728	A	20010305	ZA 2000-5728	20001017
NO 2000005669	A	20010111	NO 2000-5669	20001110
US 6713464	B1	20040330	US 2001-700094	20010102
US 2004186061	A1	20040923	US 2004-766263	20040127

APPLICANTS

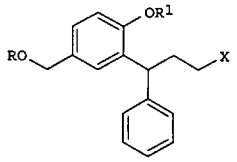
PARENT APP'N

THIS APP'N

PRIORITY APPLN. INFO.:

EP 1998-108608	A	19980512
EP 1999-924929	A3	19990511
WO 1999-EP3212	W	19990511
US 2001-700094	A1	20010102

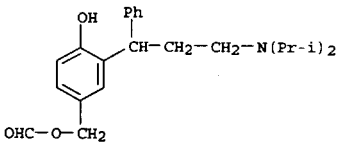
OTHER SOURCE(S): MARPAT 131:336818
GI



I

AB Title compds. (I; R = H, Me, Et, Pr, Me2CH, Bu, iso-Bu, pentyl, hexyl, PhCH2, alkyl, CHO, Ac, propionyl, isobutyryl, aminocarbonyl, aminosulfonyl, MeO2C, etc.; R1 = H, Me, Et, Pr, Me2CH, Bu, iso-Bu, pentyl, hexyl, PhCH2, alkyl, phenylalkyl; Z = NR8R9; R8, R9 = hydrocarbyl; NR8R9 = atoms to form a ring; with a proviso), were prepared as antimuscarinic agents (no data). Thus, 4-bromophenol, cinnamoyl chloride, and Et3N were stirred 18 h in CH2Cl2 to give 99.8% 3-phenylacrylic acid 4-bromophenyl ester. This was refluxed 2 h with HOAc/H2SO4 to give 43.8% 6-bromo-4-phenylchroman-2-one. The latter was refluxed with benzyl bromide, K2CO3, and NaI in acetone/MeOH to give 102.1% crude Me 3-(2-benzyloxy-5-bromophenyl)-3-phenylpropionate, which was stirred with LiAlH4 in THF to give 96.3% 3-(2-benzyloxy-5-bromophenyl)-3-phenylpropan-1-ol. This was stirred with tosyl chloride and pyridine in CH2Cl2 for 18 h to give 93.6% tosylate ester, which was refluxed 97 h with diisopropylamine in MeCN to give 77.9% [3-(2-benzyloxy-5-bromophenyl)-3-phenylpropyl]diisopropylamine. The latter was converted in several steps to 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenol, which was acylated to give I.

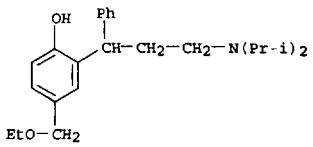
IT **250214-62-1P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,3-diphenylpropylamines as antimuscarinic agents)
RN 250214-62-1 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, α-formate (9CI) (CA INDEX NAME)



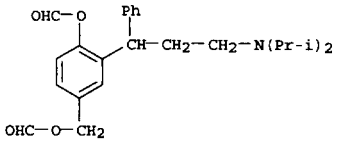
IT **214601-24-8P 250214-51-8P 250214-57-4P**
250214-58-5P 250214-69-8P 250214-70-1P
250214-71-2P 250214-72-3P 250214-73-4P
250214-74-5P 250214-78-9P 250214-79-0P
250214-85-8P 250214-86-9P 250214-87-0P
250214-94-9P 250215-00-0P 250215-01-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,3-diphenylpropylamines as antimuscarinic agents)

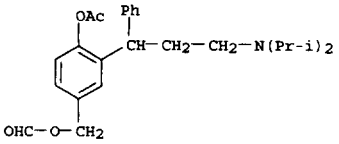
RN 214601-24-8 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(ethoxymethyl)-(9CI) (CA INDEX NAME)



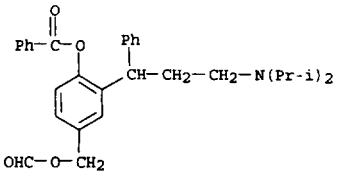
RN 250214-51-8 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(formyloxy)-, formate (ester) (9CI) (CA INDEX NAME)



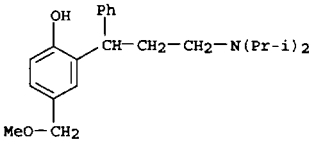
RN 250214-57-4 CAPLUS
CN Benzenemethanol, 4-(acetyloxy)-3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-, formate (ester) (9CI) (CA INDEX NAME)



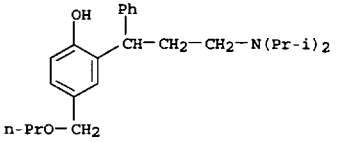
RN 250214-58-5 CAPLUS
CN Benzenemethanol, 4-(benzoyloxy)-3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-, formate (ester) (9CI) (CA INDEX NAME)



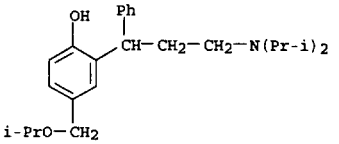
RN 250214-69-8 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(methoxymethyl)-(9CI) (CA INDEX NAME)



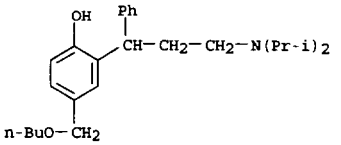
RN 250214-70-1 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(propoxymethyl)-(9CI) (CA INDEX NAME)



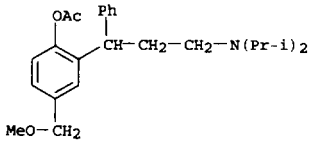
RN 250214-71-2 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-[(1-methylethoxy)methyl]- (9CI) (CA INDEX NAME)



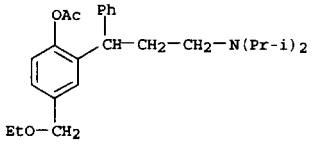
RN 250214-72-3 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(butoxymethyl)-(9CI) (CA INDEX NAME)



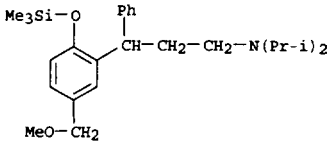
RN 250214-73-4 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(methoxymethyl)-, acetate (ester) (9CI) (CA INDEX NAME)



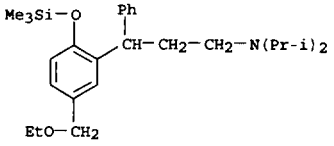
RN 250214-74-5 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(ethoxymethyl)-, acetate (ester) (9CI) (CA INDEX NAME)



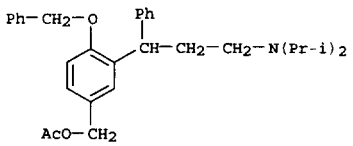
RN 250214-78-9 CAPLUS
CN Benzenepropanamine, 5-(methoxymethyl)-N,N-bis(1-methylethyl)-γ-phenyl-2-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)



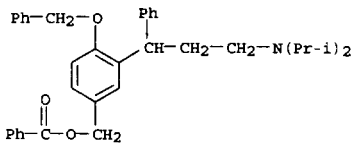
RN 250214-79-0 CAPLUS
CN Benzenepropanamine, 5-(ethoxymethyl)-N,N-bis(1-methylethyl)-γ-phenyl-2-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)



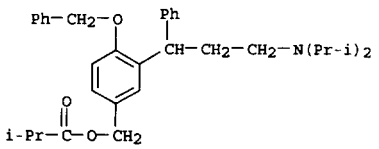
RN 250214-85-8 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, acetate (ester) (9CI) (CA INDEX NAME)



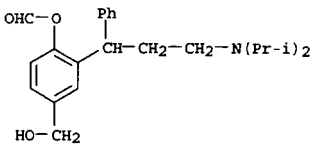
RN 250214-86-9 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, benzoate (ester) (9CI) (CA INDEX NAME)



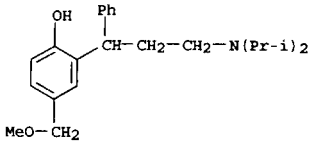
RN 250214-87-0 CAPLUS
CN Propanoic acid, 2-methyl-, [3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)phenyl]methyl ester (9CI) (CA INDEX NAME)



RN 250214-94-9 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(formyloxy)- (9CI) (CA INDEX NAME)

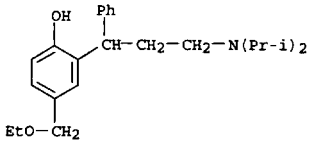


RN 250215-00-0 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(methoxymethyl)-, hydrochloride (9CI) (CA INDEX NAME)



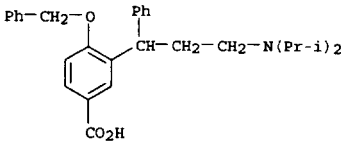
● HCl

RN 250215-01-1 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(ethoxymethyl)-, hydrochloride (9CI) (CA INDEX NAME)



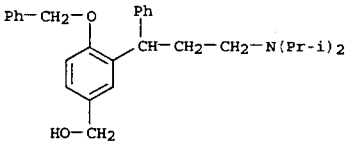
● HCl

IT **250214-38-1P 250214-39-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3,3-diphenylpropylamines as antimuscarinic agents)
RN 250214-38-1 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 250214-39-2 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

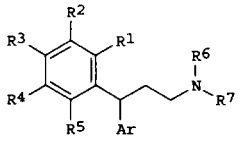
L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:682217 CAPLUS
DOCUMENT NUMBER: 129:316029
TITLE: Novel 3-aryl-3-phenylpropanamines with anticholinergic activity, their use in the treatment of urinary incontinence, and their preparation
INVENTOR(S): Johansson, Rolf; Haraldsson, Martin; Ringberg, Erik; Vagberg, Jan; Beierlein, Katarina; Emond, Rikard; Sjoberg, Birger
PATENT ASSIGNEE(S): Pharmacia and Upjohn AB, Swed.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

NOT PRIOR ART

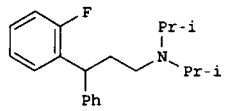
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843942	A1	19981008	WO 1998-SE556	19980326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9802478	A	19981008	ZA 1998-2478	19980324
CA 2284977	AA	19981008	CA 1998-2284977	19980326
AU 9867552	A1	19981022	AU 1998-67552	19980326
AU 739186	B2	20011004		
BR 9808069	A	20000308	BR 1998-8069	19980326
EP 1019358	A1	20000719	EP 1998-912864	19980326
EP 1019358	B1	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001522355	T2	20011113	JP 1998-541548	19980326
AT 239693	E	20030515	AT 1998-912864	19980326
PT 1019358	T	20030930	PT 1998-912864	19980326
ES 2199433	T3	20040216	ES 1998-912864	19980326
TW 555735	B	20031001	TW 1998-87105376	19980409
NO 9904438	A	19991126	NO 1999-4438	19990913
MX 9908862	A	20000228	MX 1999-8862	19990927
US 6313132	B1	20011106	US 1999-381868	19990927

PRIORITY APPLN. INFO.: SE 1997-1144 A 19970327
WO 1998-SE556 W 19980326

OTHER SOURCE(S): MARPAT 129:316029
GI



I



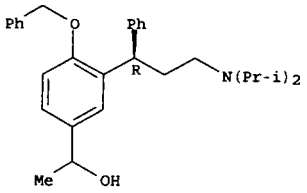
II

AB The invention relates to novel compds. I [wherein R1 = H, OH, alkyl, alkoxy, CF3, amino, alkanoylamino, alkanoyloxy, halo, hydroxyalkyl; R2, R3 = H, OH, alkyl, alkoxy, hydroxyalkyl, halo, carbamoyl, etc.; R4 = (un)substituted alkyl or amino, CHO, CO2H, NO2, cyano, N3, alkoxy, and may also be H, Me, OMe, etc. under some circumstances; R5 = H, halo, alkyl; Ar = (un)substituted (hetero)aryl; R6, R7 = hydrocarbyl with optional OH groups or O bridge(s), and may form a ring; with several provisos], their salts with physiol. acceptable acids, their racemic mixts., and the individual enantiomers. The compds. have anticholinergic activity, and in particular are of use in the treatment of urinary incontinence. Sixty synthetic examples are given, and approx. 90 compds. (including free bases and salts) were prepared and/or claimed. For instance, Wittig-type reaction of (EtO)2P(O)CH2CON(Pr-iso)2 with 2-fluorobenzophenone, followed by hydrogenation of the formed olefin and reduction of the amide with LiAlH4, gave after acidification, title compound II.HCl. In a test for inhibition of carbachol-induced contraction of isolated guinea pig bladder strips, II had a KB value of 10 nM, and other compds. had values ranging from 1.18 nM to 3315 nM.

IT **214601-51-1P 214601-52-2P 214601-53-3P**
214601-61-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of arylphenylpropanamines as anticholinergic agents)

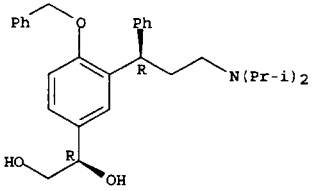
RN 214601-51-1 CAPLUS
CN Benzenemethanol, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-α-methyl-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



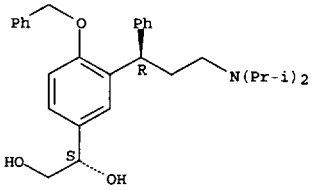
RN 214601-52-2 CAPLUS
CN 1,2-Ethanediol, 1-[3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)phenyl]-, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

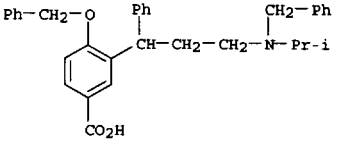


RN 214601-53-3 CAPLUS
CN 1,2-Ethanediol, 1-[3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)phenyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



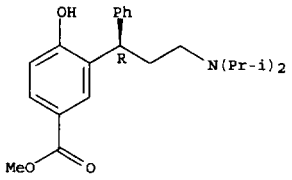
RN 214601-61-3 CAPLUS
CN Benzoic acid, 3-[3-[(1-methylethyl)(phenylmethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



IT **214600-45-0P 214600-58-5P 214601-16-8P**
214601-17-9P 214601-24-8P 214602-05-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylphenylpropanamines as anticholinergic agents)

RN 214600-45-0 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)

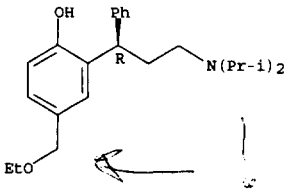
Absolute stereochemistry. Rotation (-).



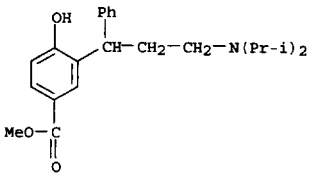
● HCl

RN 214600-58-5 CAPLUS
CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(ethoxymethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

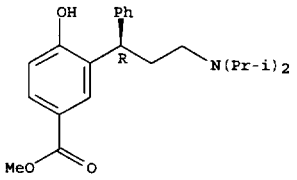


RN 214601-16-8 CAPLUS
CN Benzoic acid, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

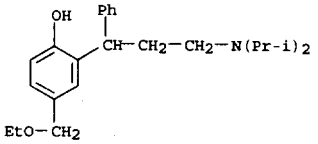


RN 214601-17-9 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 214601-24-8 CAPLUS
CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(ethoxymethyl)- (9CI) (CA INDEX NAME)

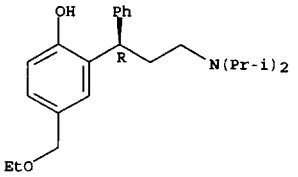


RN 214602-05-8 CAPLUS
CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(ethoxymethyl)-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 214600-58-5
CMF C24 H35 N O2

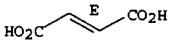
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



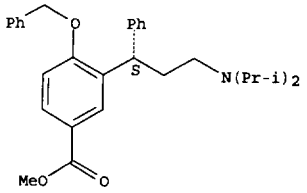
IT **156755-34-9**
RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of arylphenylpropanamines as anticholinergic agents)

RN 156755-34-9 CAPLUS

CN Benzoic acid, 3-[(1S)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:393013 CAPLUS

DOCUMENT NUMBER: 129:156415

TITLE: Biotransformation of tolterodine, a new muscarinic receptor antagonist, in mice, rats, and dogs

AUTHOR(S): Andersson, Stig H. G.; Lindgren, Anders; Postlind, Hans

CORPORATE SOURCE: Department of Drug Metabolism, Pharmacia & Upjohn AB, Uppsala, S-751 82, Swed.

SOURCE: Drug Metabolism and Disposition (1998), 26(6), 528-535
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

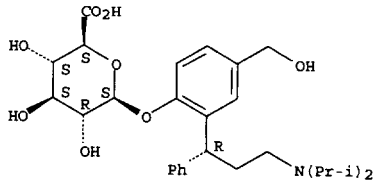
AB Tolterodine is intended for the treatment of urinary urge incontinence and other symptoms associated with an overactive bladder. The in vivo metabolism of 14C-labeled tolterodine was investigated in rats, mice, and dogs by anal. of blood and urine samples, whereas in vitro metabolism studies were performed by incubation of [14C]tolterodine with mouse, rat, dog, and human liver microsomes in the presence of NADPH. Tolterodine was extensively metabolized in vivo. Mice and dogs showed similar metabolite patterns, which correlated well with that observed in humans. In these species, tolterodine was metabolized along 2 different pathways, with the more important being the stepwise oxidation of the 5-Me group to yield the 5-hydroxymethyl metabolite of tolterodine and then, via the aldehyde, the 5-carboxylic acid metabolite. The other pathway involved dealkylation of the nitrogen. In the subsequent phase II metabolism, tolterodine and the metabolites were conjugated with glucuronic acid to various degrees. Rats had a more extensive metabolism and a markedly different metabolite pattern, with metabolites also being formed by hydroxylation of the nonsubstituted benzene ring. Gender differences were also observed, with male rats showing more extensive metabolism than females. Incubation of [14C]tolterodine yielded 5 metabolites with rat microsomes and 3 metabolites with mouse, dog, and human microsomes. The 5-hydroxymethyl metabolite of tolterodine and N-dealkylated tolterodine were major metabolites in all incubations, representing 83-99% of total metabolism Although the extent of metabolism varied among the species, the metabolic profiles were similar. Rat liver microsomes also formed metabolites hydroxylated in the nonsubstituted benzene ring. Thus, the metabolism of tolterodine in mice and dogs corresponds to that observed in humans, whereas rats have a different metabolite pattern.

IT **210573-52-7 210573-53-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(tolterodine biotransformation in mice, rats, dogs and humans)

RN 210573-52-7 CAPLUS

CN β-D-Glucopyranosiduronic acid, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(hydroxymethyl)phenyl (9CI) (CA INDEX NAME)

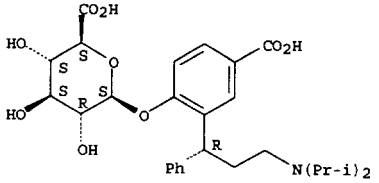
Absolute stereochemistry.



RN 210573-53-8 CAPLUS

CN β-D-Glucopyranosiduronic acid, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-carboxyphenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:508197 CAPLUS

DOCUMENT NUMBER: 121:108197

TITLE: Preparation of 3,3-diphenylpropylamines and their use

INVENTOR(S): Johansson, Rolf Arne; Moses, Pinchas; Nilverbant, Lisbeth; Sparf, Bengt Aake

PATENT ASSIGNEE(S): Kabi Pharmacia AB, Swed.

SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

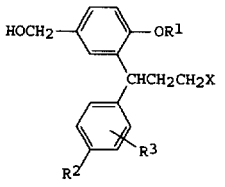
102(b)

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9411337	A1	19940526	WO 1993-SE927	19931105
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2148827	AA	19940526	CA 1993-2148827	19931105

AU 9454380	A1	19940608	AU 1994-54380		19931105
AU 672458	B2	19961003			
EP 667852	A1	19950823	EP 1993-924876		19931105
EP 667852	B1	19980408			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 08503208	T2	19960409	JP 1994-511977		19931105
JP 3343256	B2	20021111			
HU 72742	A2	19960528	HU 1995-1329		19931105
AT 164828	E	19980415	AT 1993-924876		19931105
ES 2117155	T3	19980801	ES 1993-924876		19931105
FI 9502179	A	19950505	FI 1995-2179		19950505
NO 9501775	A	19950505	NO 1995-1775		19950505
US 5559269	A	19960924	US 1995-432113		19950505
US 5686464	A	19971111	US 1996-684638		19960722
PRIORITY APPLN. INFO.:			SE 1992-3318	A	19921106
			WO 1993-SE927	W	19931105
			US 1995-432113	A3	19950505

OTHER SOURCE(S): MARPAT 121:108197
GI



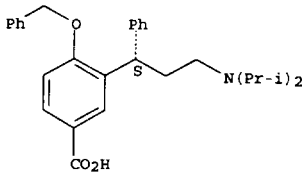
I

AB Title compds. I (R1 =H, Me; R2, R3 = H, Me, MeO, HO, H2NCO, H2NSO2, halo; X = R4R5N wherein R4, R5 = non-aromatic hydrocarbyl and which together contain at least three carbon atoms, or R4R5N = heterocyclyl), salts, optical isomers, racemic mixture and individual enantiomers are useful as anticholinergics. P-Br-C6H4OH, PhCH:CHCO2H, AcOH and H2SO4 were refluxed to give 6-bromo-4-phenyl-3,4-dihydrocoumarin which was converted in 4 steps to N,N-diisopropyl3-(2-benzyloxy-5-brophenyl)-3-phenylpropylamine (II). II was resolved to the (-)-isomer and converted in 4 steps to (-)-I [R1 = PhCH2, R2 = R3 = H, X = (Me2CH)2N].(-) mandelate salt (III). In tests for anticholinergic effect, III produced a dose-dependent inhibition of the acetylcholine-induced effect on the bladder which was about 10 times more efficient than that of a prior art analog.

IT **156755-32-7P 156755-33-8P 156755-34-9P 156755-35-0P 156755-36-1P 156755-37-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of anticholinergics)

RN 156755-32-7 CAPLUS
CN Benzoic acid, 3-[(1S)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)

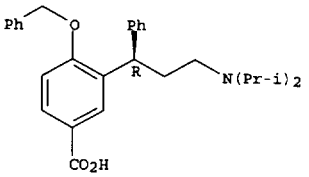
Absolute stereochemistry. Rotation (+).



● HCl

RN 156755-33-8 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)

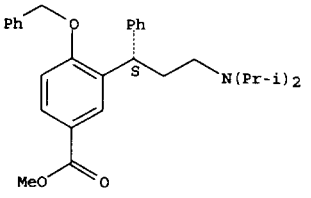
Absolute stereochemistry. Rotation (-).



● HCl

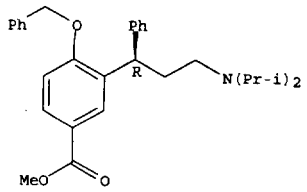
RN 156755-34-9 CAPLUS
CN Benzoic acid, 3-[(1S)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



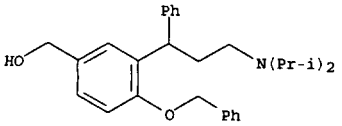
RN 156755-35-0 CAPLUS
CN Benzoic acid, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



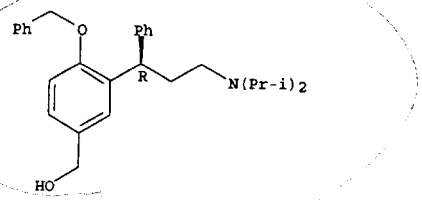
RN 156755-36-1 CAPLUS
CN Benzenemethanol, 3-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



RN 156755-37-2 CAPLUS
CN Benzenemethanol, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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Connection closed by remote host